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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/867,612	06/02/97	WANG Y	ALX-149

HM11/1105

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EXAMINER	
CUNNINGHAM, T	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 11/05/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Notice of Abandonment

Application No.	Applicant(s)
08/867,612	Wang et al.
Examiner	**Group Art Unit**
Thomas Cunningham	1644

This application is abandoned in view of:

☑ applicant's failure to timely file a proper response to the Office letter mailed on 3/31/98.

- ☐ A response (with a Certificate of Mailing or Transmission of _____) was received on _____, which is after the expiration of the period for response (including a total extension of time of ____ month(s)) which expired on _____.
- ☐ A proposed response was received on _____, but it does not constitute a proper response to the final rejection.

  (A proper response to a final rejection consists only of: a timely filed amendment which places the application in condition for allowance; a Notice of Appeal; or the filing of a continuing application under 37 CFR 1.62 (FWC)).
- ☐ No response has been received.

☐ applicant's failure to timely pay the required issue fee within the statutory period of three months from the mailing date of the Notice of Allowance.

- ☐ The issue fee (with a Certificate of Mailing or Transmission of _____) was received on _____.
- ☐ The submitted issue fee of $_____ is insufficient. The issue fee required by 37 CFR 1.18 is $_____.
- ☐ The issue fee has not been received.

☐ applicant's failure to timely file new formal drawings as required in the Notice of Allowability.

- ☐ Proposed new formal drawings (with a Certificate of Mailing or Transmission of _____) were received on _____.
- ☐ The proposed new formal drawings filed _____ are not acceptable.
- ☐ No proposed new formal drawings have been received.

☐ the express abandonment under 37 CFR 1.62(g) in favor of the FWC application filed on _____.

☐ the letter of express abandonment which is signed by the attorney or agent of record, the assignee of the entire interest, or all of the applicants.

☐ the letter of express abandonment which is signed by an attorney or agent (acting in a representative capacity under 37 CFR 1.34(a)) upon the filing of a continuing application.

☐ the decision by the Board of Patent Appeals and Interferences rendered on _____ and because the period for seeking court review of the decision has expired and there are no allowed claims.

☒ the reason(s) below:

Attorney was notified that Notice of Abandonment would be mailed, but that petition for revival and CPA request had already been received.

TC

THOMAS M. CUNNINGHAM
PRIMARY EXAMINER
GROUP 1800

1. Applicants' comments regarding the drawing requirements is noted. Formal drawings will be required upon the identification of allowable subject matter. The amendment filed on 4/10/97, paper #11 remains not entered in this application since Applicant did not request its entry in the file wrapper continuation request filed on 6/2/97. This application is a file wrapper continuation of application serial number 08/311489, filed 9/23/94. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a)

2. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

   A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

   Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

3. Claims 1-14 are rejected under 35 U.S.C. § 103 as being unpatentable over Sindelar et al. ('499) in view of Auda et al. (Rheumatol. Int.), Wurtzer et al. (Complement Inflamm.), and Montz et al. (Cell. Immunol.). Claims 1-14 are drawn to methods for the treatment of established joint inflammation comprising the administration of an effective amount of a C5 blocker which does not block the functions of early complement components and further comprising the determination of the C5a and/or C5b level through ELISA assays or chemotactic assays to evaluate the patient's response to the treatment protocol. The patent teaches methods for the treatment of established joint inflammation comprising the administration of an effective amount of a C5 blocker. The invention of '499 is taught to be useful in the treatment of inflammatory disorders, such as rheumatoid arthritis, through the selective inhibition of C5 (see Table 3, claims 3-13, columns 5-10, and columns 22-23). Rheumatoid arthritis is considered an established joint inflammation, i.e. an inflammatory disease (see specification, page 11). By inhibiting the cleavage of C5, the inhibitors of '499

substantially inhibit the cell-lysing ability of complement in the serum of a patient as well as chemotactic attraction of cells involved in the inflammatory response (see Montz et al.). The method of the '499 patent would also substantially reduce the level of C5b-9 in the plasma of a patient because the compounds of the '499 patent inhibit the cleavage and activation of C5 into C5a and C5b. According to Figures 2-3 of the '499 patent, the compounds of the patent are capable of reducing the cell lysing ability of complement by at least 10% as well as the amount of C5a by at least 10%. The blockers of the '499 patent also do not appear to substantially interfere with the cleavage of C3 (see Figure 2). The reference differs from the claimed invention in that a C5 inhibitor which did not effect the early C components is not taught. Wurzner et al. and Montz et al. teach C5 inhibitors which do not effect the early C components. These C5 inhibitors are C5 specific antibodies. By blocking C5 activation, one of ordinary skill in the art would have recognized that the chemotactic effects of C5 would be blocked as would the ability of the molecule to stimulate the oxidative burst in monocytes and neutrophils. Such chemotaxis and oxidative burst is associated with tissue injury in inflammatory joint disease (see Sindelar, columns 4-6). Therefore, one skilled in the art would have been motivated to treat inflammatory joint diseases with compounds capable of specifically disrupting the inflammatory response, such as C5 inhibitors). Auda et al. teach the measurement of complement activation products in patients suffering chronic rheumatic diseases and that such measurements provide additional information which allows for the prediction of patient clinical status (see Discussion). Auda further teach that the monitoring of C5b-9 levels in patients may provide for a more sensitive indicator or patient status than other indicators of disease status (Discussion, page 188, last 2 paragraphs). Such an assay would allow for the measurement of C5b levels within the C5b-9 complexes. Wurzner teaches the inhibition of terminal C components by monoclonal antibodies which are specific for C5 (see Abstract and Discussion). Wurzner teaches the production of specific tools (i.e., antibodies) which influence the formation or MAC and the activation of C5.

One of ordinary skill in the art at the time the invention was made would have been motivated to use the modify the teachings of Sindelar et al. with the teachings of Auda et al., Montz et al., and Wurzner et al. to arrive at a method of inhibiting inflammatory joint disease through the administration of C5 inhibitory antibodies and to determine the levels of C5a and/or C5b in the fluid samples of patients being treated according to the teachings of Sindelar in order to determine the clinical status of the patients so treated. One of ordinary skill in the art would have recognized that inhibitory antibodies were analogous to the compounds taught in Sindelar for the inhibition of C5 activation and that such inhibition of C5 would have reduced the inflammatory response by reducing infiltration of PML. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as

evidenced by the references, especially in the absence of evidence to the contrary.

Applicants' traversal of the previous rejection made under 35 USC 103 is noted. In view of the new grounds of rejection, necessitated by the amendment to the claims, it is considered moot. However, as the arguments relate to the present rejection, they will be addressed. It appears that Applicant argues that the Sindelar patent is not enabled, stating that "Surely, workers of ordinary skill in the art did not reasonably expect that these compounds would successfully treat all of the listed disease conditions." This argument is noted, however Applicant is reminded that the claims of all issued patents bear a presumption of validity, i.e. enablement, novelty, and non-obviousness. See 35 U.S.C. §282. In this case, the claims of Sindelar bear a presumption of validity with respect to the treatment of patients having undesirable or inappropriate complement activity (i.e. patients suffering from rheumatoid arthritis, such patients being art recognized to have abnormal levels of complement activation products, see Auda et al., entire document, especially Results). The declaration filed has also been considered but not found persuasive in view of Auda et al. which clearly indicates the involvement of complement in rheumatoid arthritis and the recruitment of PML. This teaching would have led one of ordinary skill in the art to recognize that inflammatory joint disease would have been treated through the inhibition of complement activation and prevention of C5 activation (to prevent the initiation of C5a mediated chemotaxis of cells).

4. No claim is allowed. This application is a file wrapper continuation of application serial number 08/311489, filed 9/23/94. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

5. Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). THE CM1 FAX CENTER TELEPHONE NUMBER IS (703) 308-4242

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher Eisenschenk whose telephone number is (703) 308-0452. The examiner can normally be reached Monday through Thursday from 6:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 180 receptionist whose telephone number is (703) 308-0196.

March 30, 1998
Christopher Eisenschenk, Ph.D.
Primary Examiner
Group 1800

C Eisenschenk